UNITED STATES PATENT AND TRADEMARK OFFICE

KP

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/942,586	08/31/2001	James Hager	571-737	9428

7590 09/25/2003

H. Samuel Frost
Bereskin & Parr
Box 401
40 King Street West
Toronto, ON M5H 3Y2
CANADA

EXAMINER	
JOHNSTON, PHILLIP A	

ART UNIT	PAPER NUMBER
2881	

DATE MAILED: 09/25/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

PTO-90C (Rev. 07-01)

Office Action Summary	Application No.	Applicant(s)
	09/942,586	HAGER, JAMES
	Examiner	Art Unit
	Phillip A Johnston	2881

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on _02 July 2003_ .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) _1-23_ is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) _1-23_ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on _31 August 2001_ is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _4_ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Detailed Action

Claims Rejection - 35 U.S. C. 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. Claims 1-5, and 7-10 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Whitehouse, U. S. Patent No. 6,188, 066.

Whitehouse discloses a multipole ion guide, which is used to transport ions entering vacuum from an API source to non-dispersion type mass analyzers. A range of ion mass to charge (m/z) can be efficiently transmitted through a multipole ion guide provided the ion guide operating stability region is set to pass those values of m/z. If an ion with a given mass to charge ratio falls within the operating stability region set for a multipole ion guide, the ion will be effectively trapped from drifting to far in the off axis direction but is free to move in the direction of ion guide axis. See Column 3, line 51-61. The offset potential of the multipole lens, that is the DC voltage applied uniformly to all the rods on

which the AC and alternate polarity DC rod potentials are floated and referenced is one variable that can to be used to set the energy of ions transmitted through the multipole ion guide. See Column 4, line 10-14.

Whitehouse teaches that a valuable feature of multipole ion guides when operated in higher background pressures is that ions traversing the length of the ion guide experience a number of collisions with the background gas resulting in the cooling of the ion kinetic energy, as recited in Claim 3. As the ions enter the multipole ion guide and are transmitted through it, the RF or combined RF-DC field effectively traps the ions from dispersing in the radial direction due to collisions with the background gas yet permits movement of ions in the axial direction often driven by the gas dynamics. Ions which experience a number of low energy collisions with the neutral gas within the multipole rod assembly have their kinetic energy reduced resulting in a narrowing of the ion energy spread for those ions which exit the multipole rods, as recited in Claim 2. The number of collisions an ion experiences as it travels the length of the ion guide is a function of the rod length and the background pressure inside the rods. If the relative voltages of the capillary exit lens 50, ring lens 51, skimmer 47 and the multipole ion guide 40 DC offset potential remain the same then the ions entering the multipole ion guide will have similar energy spreads and will be transmitted to the exit of the multipole ion guide with the same efficiency. See column 13, line 9-30.

Whitehouse further shows in FIG. 11, a three vacuum pumping stage API/ion trap system, as recited in Claim 5, where a multipole ion guide begins in vacuum pumping stage 148 and extends continuously through the three vacuum pumping stages. See Column 19, line 24-28. In addition, the multipole ion guide 165 can efficiently transport ions through gradient in background gas pressure. As was shown in FIGS. 8a, b and c, the ion energy spread is reduced due to ion collisional cooling with the background gas. Higher trapping efficiency can be achieved with ions entering ion trap 154 when the ions have a narrow energy spread. Increased trapping efficiencies result in higher signal sensitivity for a given ion current entering trap 154. The ability to selectivity cutoff a range of m/z transmission through multipole ion guide 165 can also be used to increase sensitivity in ion trap mass spectrometers. Ion traps must first trap ions and then conduct a mass analysis on a packet of trapped ions. The trap can only hold a limited number of ions before it suffers from space charge effects, which can shift measured m/z values and deteriorate resolution. See Column 20, line 19-33.

3. Claims 6, 11-14, and 22 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Whitehouse, U. S. Patent No. 6,188, 066, as applied above.

Whitehouse teaches that the ability of a multipole ion guide to deliver an ion beam with low energy spread and where the mean energy and m/z range can be adjusted into a mass analyzer can be used to improve the

performance of an API/Time-Of-Flight, API/Ion Trap and API/FT-ICR mass spectrometer systems, as recited in Claims 6, 8,10-14, and 22. See Column 4, line 16-21.

Whitehouse further discloses an Electrospray ion source interfaced to a quadrupole mass spectrometer is diagramed in FIG. 1. The system shown includes four vacuum pumping stages and a static voltage lens configuration to transfer ions through the first three pumping stages and focus them into the entrance of quadrupole mass spectrometer 18. An electrostatic field is applied between the capillary exit 8, the ring lens 9 and the first skimmer 10 to electrostatically focus and accelerate ions through the skimmer 10 orifice 11 and on into the second vacuum stage 12. Electrostatic potentials are maintained between skimmers 10 and 13 and a portion of the ions passing through skimmer 10 are focused through orifice 22 in skimmer 13 into the third vacuum pumping stage 20. Potentials are set on electrostatic lens elements 14, 15 and 16 to focus ions through aperture 17 after which they pass into the quadrupole mass filter 18 located in the fourth pumping stage 24. See Column 7, line 57-63, and Column 8, line 18-33.

4. Claims 15-21, and 23 are also rejected under 35 U.S.C. 102(b) as being clearly anticipated by Whitehouse, U. S. Patent No. 6,188, 066, as applied above.

Whitehouse discloses that the ion energy relative to the quadrupole mass filter offset voltage is established by a combination of acceleration energy imparted by the expanding carrier gas and the electrostatic potentials applied. The capillary exit 8

potential relative to the ring electrode 9 and skimmer electrode 10 can be set high enough to cause Collisional Induced Dissociation (CID) which can affect the energy and energy spread of the parent and fragment ions. See Column 8, line 37-44.

Whitehouse also teaches that the collisional cross sections of ions generated by API sources are not always known, however. In particular, the cross section of multiply charged ions which can be produced in the electrospray ion source are not always known. Consequently, for a given multipole ion guide configuration, values of a_n and q_n where efficient ion transmission through the multipole lens can be achieved must be mapped for any given m/z and background pressure combination encountered. See Column 10, line 33-42.

Whitehouse further discloses that the ability of the multipole ion guide to selectively transmit a range of m/z values while cutting off the transmission of m/z outside that range can be used to increase the duty cycle and detector sensitivity in an API/TOF system. If a DC potential is applied to the poles where each adjacent pole has opposite DC polarity, the a_n and q_n values can be selected so that the multipole ion guide will pass a narrower range of m/z. See Column 17, line 24-36.

Whitehouse further teaches that one variable which effects duty cycle in a TOF instrument is the repetition rate at which ions are pulsed in the flight tube, accelerated and detected. Assuming that the pulsing region 135 can refill between pulses, that is the primary ion beam 134 energy is set to satisfy this criteria, the pulsing repetition rate will be limited by the fastest flight time of the lowest m/z ion and

the slowest flight time of the highest m/z ion in consecutive ion packets traveling through flight tube 127 to the detector. Any overlap of ions from one pulsed packet to the next will increase the difficulty in interpreting the resulting mass spectrum. If ions of lower or higher m/z were not of interest in a given analysis, those ions could be preventing from entering the pulsing region by selecting an appropriate a_n and q_n value for the multipole rod 18 operation. By reducing the arrival time spread of an ion packet as it travels down the flight tube, the time in between pulses can be reduced resulting in an increase in duty cycle. See Column 17, line 46-62.

Examiners Response to Arguments

5. Applicant's arguments filed 7-2-2003 have been fully considered but they are not persuasive.

Argument 1

Applicant states, that "Whitehouse does not describe or even suggest selecting between ion (or groups of ions) based on their charge state."

The applicant is respectfully directed to paragraph [0006] in applicants specification, which states; The present invention provides a method for enhancing the appearance of multiply charged ions in the single MS survey scan by first ensuring the

ions have substantially similar energies, preferably by collisional cooling, and then differentiating between the different ions by an energy barrier. These steps are preferably carried out in an ion trap, most preferably when utilizing a linear ion trap. The technique involves first allowing the trapped ions to cool via collisions with a background gas to the point where singly and multiply charged ions have the similar kinetic energies. Subsequently a normally repulsive DC barrier voltage at one end of the linear ion trap, previously used to maintain the trap, is reduced to a level where the singly charged ions are allowed to escape while the multiply charged ions remain trapped.

The applicant is also respectfully directed to Whitehouse (066), Column 5, line 45-50, which states; a valuable feature of multipole ion guides when operated in higher background pressures is that ions traversing the length of the ion guide experience a number of collisions with the background gas resulting in the cooling of the ion kinetic energy. As the ions enter the multipole ion guide and are transmitted through it, the RF or combined RF-DC field effectively traps the ions from dispersing in the radial direction due to collisions with the background gas yet permits movement of ions in the axial direction often driven by the gas dynamics. Ions, which experience a number of low energy collisions with the neutral gas within the multipole rod assembly have their kinetic energy reduced resulting in a narrowing of the ion energy spread for those ions which exit the multipole rods. The number of collisions an ion experiences as it travels the length of the ion guide is a function of the rod length and the background pressure inside the rods. If the relative voltages of the capillary exit lens 50, ring lens 51,

skimmer 47 and the multipole ion guide 40 DC offset potential remain the same then the ions entering the multipole ion guide will have similar energy spreads and will be transmitted to the exit of the multipole ion guide with the same efficiency. With the relative upstream lens potentials held constant with the ion guide DC offset potential, the ion kinetic energy cooling due to collisions will remain consistent as the multipole DC offset potential is adjusted. Consequently, with a multipole ion guide operated in a higher vacuum pressure region where ion collisional cooling occurs, the narrow energy spread of the ions can be maintained independent of changes in the mean ion energy when the ion guide DC offset potential is adjusted.

To illustrate this point, the energy spread of a doubly charged Gramicidin S $(M+2H)^{+2}$ ion (m/z 571) was measured by ramping the voltage of lens 53 in FIG. 2 while monitoring the mass spectrometer ion signal. This technique will not give a precise profile of ion energy because lens 53 is a focusing element as well as having the ability to apply stopping potentials. However, even though the focusing characteristics will change slightly as the voltage of 53 is ramped, the boundaries of ion energy for a given m/z can be attained.

The examiner has interpreted that ramping the voltage of lens 53 as described in the Whitehouse (066) reference above is equivalent to applying “a normally repulsive DC barrier voltage at one end of the linear ion trap, previously used to maintain the trap” as recited in the applicants specification referenced above.

The examiner has also interpreted by comparing the above reference in the applicants specification to the Whitehouse (066) reference above that both describe

the use of collisional cooling to first reduce the kinetic energy spread of the ions, and then both adjust the DC voltage at the end of the ion trap to select a specific charge state of an ion.

Conclusion

6. The Amendment filed on 7-02-2003 under 37 CFR 1.131 has been considered but is ineffective to overcome the Whitehouse (066) reference.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip A Johnston whose telephone number is 305 7022. The examiner can normally be reached on 7:30 to 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John R Lee can be reached on 703 308 4116. The fax phone numbers for the organization where this application or proceeding is assigned are 703 872 9318 for regular communications and 703 872 9319 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 308 0956.

PJ
September 9, 2003

JOHN R. LEE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 2800